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March 8, 2008

Adam Heyward
Regulatory Management Branch 2 (PM34)
Antimicrobials Division (7510P)
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 20460

SUBJECT: Request for Registration of a Manufacturing Use Product (ChitoSante' MUP) containing the Active Ingredient (Chitosan) Produced by VA&G Bioscience, Inc.; EPA Registration No. 75100-RG

Dear Adam;

On behalf of VA & G Bioscience Inc., Health & Environmental Horizons, Ltd. (US Agent) submits this request for registration of a Manufacturing Use Product containing the active ingredient chitosan. Products formulated from this MUP may be used as antimicrobials to inhibit the growth of non-health related organisms such as bacteria, mold, mildew and fungus that cause odor, stains, discoloration, decay and deterioration of the treated materials. ChitoSante' MUP may be incorporated into products used in the finishing process of manufacturing textiles, including carpet. It may be used for surface applications to floor coverings, textiles, paper, leather, textile wall partitions, vinyl, upholstery, wallboard, hard contact surfaces, and vehicle interiors. It may be used in home use products, used in washing machines, for consumer use on items such as wearing apparel, shoes and insoles, curtains, mattresses, upholstery, carpet, exercise equipment, air filters, textile covers (boat, car, sofa), and synthetic turf fields (i.e. Astroturf). ChitoSante' MUP may be used in accordance with 40CFR 180.1072 (poly-D-glucosamine), exemption from the requirement of a tolerance (4/19/95), when used as a pesticide in the production of any raw agricultural commodities.

Description of Chitosan

Chitin, which is poly-N-acetyl-D-glucosamine (re: 40CFR 180.1089), occurs naturally in a variety of crustaceans. Deacetylation of the amines results in poly-D-glucosamine, also referred to as chitosan (re: 40CFR 180.1072). The molecular weight of chitosan ranges from 100,000 to 400,000, while the individual chitosan oligomers range from 10-50,000 with an average molecular weight of 12,000.

Chitin, a major component of crustacean shells (i.e. shrimp, crab, lobster), is extracted by simple acid hydrolysis. Chitin is deproteinated and demineralized by heating in hydrochloric acid, followed by deacetylation in alkali. The resulting suspension is then centrifuged and chitosan is extracted into the supernatant. Any impurities that may have been present in the chitin as a very minor part of the suspension (material that may have been originally part of the crustacean shell) are collected in the pellet and discarded along with the non-reacted chitin. Deproteination removes any and all protein allergens, thus eliminating the concern of shellfish allergic reaction to humans. It is not manufactured by a multi-step synthetic process in which various impurities could form depending on reactants, reaction conditions, and other process parameters. There are also no biological impurities that could survive such caustic chemical treatments. There are adequate quality control and quality assurance measures throughout the manufacturing process to verify the purity, degree of deacetylation, molecular weight and other vital factors that provide chitosan with its unique antimicrobial characteristics. Each batch is screened for the presence of heavy metals and other unwanted impurities to insure they meet acceptable levels that are enforced at the Federal and State levels. The supernatant is filtered to further assure the complete removal of suspended matter. Thus, whether it is intended for use as a PGR, a biopesticide or an antimicrobial, or all three, the derivation and manufacturing processes of chitosan are identical. It is the exact same material. However, it can, and does, have multiple modes of action.

Registered Uses of Chitosan in Pesticide Products

Chitosan was originally registered to DCV, Inc. (Wilmington, DE) as a **Plant Growth Regulator** in a product called YEA! (EPA Reg. No.56437-1). Subsequently Vanson L.P. obtained an exemption from the requirement of a tolerance for chitosan when used in the production of any raw agricultural commodity (40CFR180.1072). Shortly thereafter, Solutia, Inc. obtained registration for a technical grade chitosan (EPA Reg. No. 73882-1; now CANCELLED) for industrial use as an **Antimicrobial** in treated articles. GlycoGenesys, Inc. obtained a registration for the use of chitosan as a "plant defense booster", as a **Biochemical pesticide** (Elexa 4, EPA Reg. No. 70464-3). This was subsequently transferred to Plant Defense Boosters, Inc. in 2004 (EPA Reg. No. 81045-2).

In 2003, VA&G Bioscience, Inc. requested a treated article exemption for the use of chitosan in a product called ChitoSante' (ABN: Bac-Shield) (EPA Reg. No. 75100-1). In 2006 this product was transferred to Chem-Tex Laboratories, Inc. (EPA Reg. No. 81446-1), but VA&G Bioscience continues to manufacture the product. In 2006 VA&G Bioscience developed its own manufacturing process for the production of technical grade chitosan. In December 2006 thru January 2007, they provided all of the required data/information to support its use as an alternate unregistered source of active ingredient in EPA Registration 81446-1. AD approved this alternate unregistered source of TGAI on May 24, 2007.

Thus, chitosan has been registered by EPA as a Plant Growth Regulator, an Antimicrobial, and a Biochemical Pesticide. Also, the parent acetylated compound, chitin, from which chitosan is derived, was originally registered in 1988 as a nematocide.

EPA Decisions Regarding Chitosan

EPA exempted chitin (poly-N-acetyl-D-glucosamine; re: 40CFR 180.1089) and chitosan (poly-D-glucosamine;,re: 40CFR 180.1072) from the requirement of a tolerance (4/19/95) when used as a pesticide in the production of any raw agricultural commodity "based on the nontoxic nature of this chemical". This same position was reiterated in a recent EPA document, US EPA Preliminary Work Plan (Docket No: EPA-HQ-2006-0566) for Chitin and Chitosan, Summary Document Registration Review, Initial Docket, September 2007.

Data Requirements for Registration of a Manufacturing Use Product Containing Chitosan

VA&G Bioscience, Inc. believes EPA has a full battery of data necessary to support the Section 3 registration of a Manufacturing Use Product. The Manufacturing Use grade chitosan that is produced by VA&G Bioscience, Inc. is 99.9% pure. The degree of deacetylation, viscosity, ash content, insolubles, turbidity, other chemically related factors, and source(s) of chitin (e.g. shrimp and crab) have been determined in individual batch analyses. All of these properties have been performed in accordance with ASTM methods and EPA recommended analytical standards for the individual analysis performed. More importantly, there is no difference in toxicity since the chitosan polymer produced has the same degree of deactylation and chain length as the original source of active ingredient; both sources being equivalent to pharmaceutical grade chitosan. VA&G Bioscience, Inc. has provided its own product chemistry and physical properties data to support a manufacturing use product. There are no long-term toxicology studies or other data required and therefore, we believe the analytical work performed satisfies the requirements under FIFRA.

Waiver requests for specific product chemistry/properties data and acute toxicology data are attached.

As noted above, humans are exposed to chitosan through numerous existing pathways, some of which are intentional and recommended. Chitosan is ubiquitous in nature. It is one of nature's most common organic compounds, second only to cellulose, a close cousin. Over the past decade, researchers in Japan, Europe and the U.S. have chemically modified this compound for use in bandages, burn dressings, food additives, drug capsules, and cosmetics. Scientists have begun trying out a chitin compound as an edible film for preserving the quality and texture of foods. It is taken orally as a dietary supplement by humans at dose levels far greater than anything they would be exposed to on a more casual basis from handling the manufacturing use product. We believe the extensive uses of chitosan in food processing, water purification, wastewater treatment, personal care products, biomedical products, and dietary supplements illustrate the widespread belief by almost every US regulatory authority (including EPA) that chitosan is not only safe for human use, but is recommended for human use (internally and externally). The NIH study in humans attests to the safety of chitosan to both male and female participants when administered orally at very large doses.

In April, 1995 EPA granted chitosan an exemption from the requirement of a tolerance in any raw agricultural commodity (40CFR180.1072). In that Final Rule EPA noted it is chitosan's "nontoxic nature" that has allowed "chitin-based products to be permitted in foods as hypocholesterolemic agents, as dietary fiber in low-calorie diets, and as agents to increase the specific loaf volume of bread". It is approved by EPA as a List 4B inert and USDA has evaluated the use of chitosan under the National Organic Program (NOP) regulations as an inert or adjuvant ingredient (7CFR205.601(m)). Both have reiterated their belief that "chitosan is not toxic". This same conclusion has been reiterated again by EPA in September 2007 [US EPA Preliminary Work Plan (Docket No: EPA-HQ-EPA-2006-0566) for Chitin and Chitosan]. All toxicology testing have supported this conclusion and have failed to identify any adverse effects when administered orally, dermally or via inhalation to test animals and humans (male and female). It is not a sensitizer and is non-allergenic, since there is no protein component.

Request for Waivers of Ecological Effects Data Requirements

VA&G Bioscience, Inc. requests a waiver for all ecological effects data for Chitosan. Waivers have been granted for end-use products containing chitosan as the active ingredient. The same rationale exists with respect to a Manufacturing Use Product. VA&G Bioscience, Inc. believes the waiver is justified based on: (1) its low toxicity, (2) the ubiquitous occurrence of chitosan already present in the environment (crustaceans are a primary source of this material), (3) it is a high molecular weight polymer that is poorly absorbed, (4) it is completely biodegradable, (5) it is incorporated into the structural makeup and integrity of many living organisms, (6) EPA has granted waivers for end-use products containing chitosan, and (7) chitosan is commercially available and used for storm water treatment and sediment control resulting in far greater quantities of chitosan into the environment than from its limited uses in pesticide products (e.g. tons vs lbs). The products are Storm-Klear Liqui-Floc (1% liquid form), Liqui-Floc Concentrate (2% liquid form) and Storm-Klear Gel-Floc (100% solid form). Products available from Vanson, the original manufacturer of TGAI. Chitosan has been used at the Seatac International Airport in Seatle for sediment control. Extensive environmental fate and ecological testing have been performed by Vanson (e.g. Fathead minnow, Daphnia, and Rainbow trout) supporting this use. Thus, the purposeful use of chitosan for water treatment introduces greater quantities of chitosan into the environment than from its limited uses in pesticide products.

Any further ecological effects and environmental fate testing would provide no additional useful information and should be waived. This request is consistent with previous EPA decisions to waive these data for chitosan.

Documents Being Submitted in Support of the MUP Application

Three (3) copies of supporting data and one (1) copy each of the following are attached:

- o Application for Pesticide Registration (Form 8570-1)
- o Confidential Statement of Formula (Form 8570-4), Document Number 1, Confidential Attachment)
- o Label for ChitoSante' MUP
- o Certification with Respect to Citation of Data (Form 8570-29)
- o Data Matrix, EPA Form 8570-35
- o Waiver Requests for Product Properties, Acute Toxicology, Environmental Fate and Ecological Effects Data
- o Transmittal Document

Conclusion

We believe the totality of data and information is sufficient for EPA to support a Section 3 registration for a Manufacturing Use Product containing chitosan produced by VA&G Bioscience. The integrated source of chitosan technical active ingredient has already undergone internal EPA review and approval. All data requirements have been satisfied or addressed for an integrated source of TGAI. This present request for chitosan used in an MUP necessitates that additional product chemistry data need to be addressed. These data requirements have been identified in the Data Matrix and waivers, where indicated, have been requested. We believe no additional data are necessary at this time.

We respectfully request approval of this MUP for chitosan.

Sincerely,

R. Bruce Jaeger
President

Atch: a/s

VOLUME 1 OF 2 OF SUBMISSION
TRANSMITTAL DOCUMENT

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U.S. AGENT/REPRESENTATIVE:

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REGULATORY ACTION:

Submission of Registration Application for ChitoSante´ MUP.

TRANSMITTAL DATE:

March 8, 2008

MRID NUMBER	VOLUME NUMBER	STUDY TITLE	EPA GUIDELINE Number
	1 of 2	Transmittal Document	-
47369601	2 of 2	Document Number 1: Product Identification and Disclosure of Ingredients; Certified Limits	830.1550 830.1750
47027602	2 of 2	Document Number 2: Description of Beginning Materials and Manufacturing Process	830.1600 830.1620 830.1650

47060701	2 of 2	Document Number 3: Discussion of the Formation of Impurities	830.1670
47027604	2 of 2	Document Number 4: Five Batch Analysis	830.1700
47027606	2 of 2	Document Number 6: Analytical Method	830.1800

COMPANY OFFICIAL: R. Bruce Jaeger Signature: 

COMPANY NAME: VA & G Bioscience, Inc.
COMPANY CONTACT: R. Bruce Jaeger
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